

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 15

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte FRANCES A. BOUFFARD and JAMES F. DROPINSKI

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Appeal No. 95-3387  
Application No. 08/005,942<sup>1</sup>

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ON BRIEF

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Before WINTERS, WEIFFENBACH and WEIMAR, Administrative Patent Judges.

WEIMAR, Administrative Patent Judge.

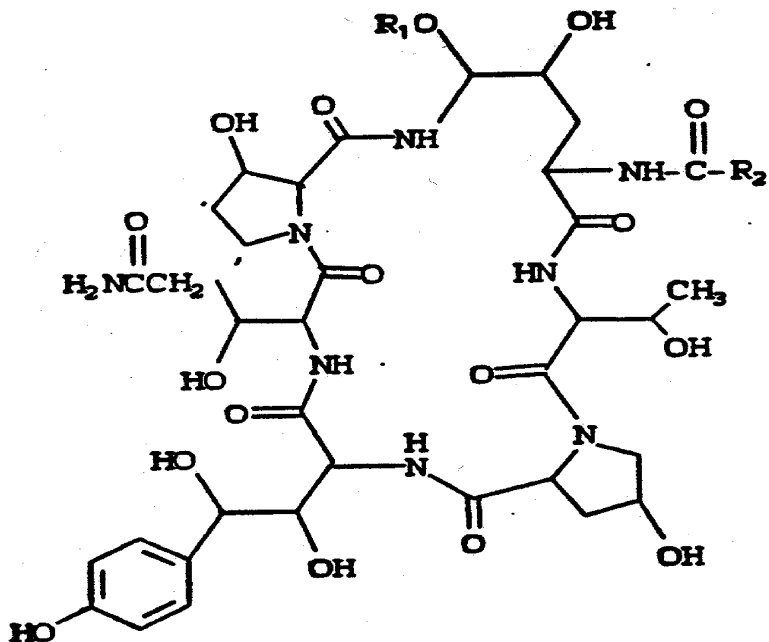
DECISION ON APPEAL

This is an appeal from the examiner's decision finally rejecting claims 1-15. Claims 1 and 12 are illustrative of the subject matter on appeal and they read as follows:

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<sup>1</sup> Application for patent filed January 15, 1993. According to the appellants, the application is a continuation-in-part of Application No. 07/775,774, filed October 17, 1991, now Patent No. 5,430,019, issued July 4, 1995, which is a continuation-in-part of Application No. 07/960,983, filed October 16, 1992, now abandoned.

**1. A compound having the formula (SEQ ID NO 1)**



**wherein:**

**R<sub>1</sub> is**

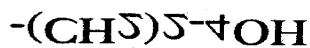
- CH<sub>2</sub>CH(NH<sub>2</sub>)CH<sub>2</sub>R<sup>I</sup>
- C<sub>n</sub>H<sub>2n</sub>NR<sup>II</sup>R<sup>III</sup>
- (CH<sub>2</sub>)<sub>1-3</sub>CH(NH<sub>2</sub>)R<sup>IV</sup> or
- C<sub>n</sub>H<sub>2n</sub>NHR<sup>V</sup>

**wherein n is 2 to 6;**

**R<sub>2</sub>** is            -C<sub>9</sub>-C<sub>21</sub> alkyl,  
                       -C<sub>9</sub>-C<sub>21</sub> alkenyl,  
                       -C<sub>1</sub>-C<sub>10</sub> alkoxyphenyl, or

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սուր Բրաշնացենիցայիլ յստեղարթե շարժ քրեթօլ:



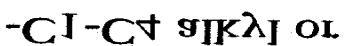
Б<sub>А</sub> !2



Б<sub>ІА</sub> !2



Б<sub>III</sub> !2



Б<sub>II</sub> !2



Б<sub>I</sub> !2



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The references relied upon by the examiner are:

Schmatz	5,166,135	Nov. 24, 1992
Sandoz (Belgium) '310 Pat.	851,310	Aug. 10, 1977
Sandoz (Belgium) '067 Pat.	859,067	Mar. 28, 1978
Michel (German) '130 Pat.	2,065,130	June 24, 1981

Claims 1-15 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as lacking patentable distinction over (1) Claims 1-17 or (2) Claims 1-4 or (3) Claims 3-20 or (4) Claims 4-7 or (5) Claims 1-11 and 13 or (6) Claims 1-10 or (7) Claims 1-9 of copending applications (1) 07/936,558; (2) 07/963,332; (3) 07/775,774; (4) 07/960,983; (5) 07/936,531; (6) 07/936,434; and (7) 07/959,948; respectively. We affirm this rejection.

Claims 1-15 stand rejected under 35 U.S.C. § 103 over Schmatz alone or in the alternative over '310 Pat. or '067 Pat. in combination with Michel. We reverse this rejection.

#### BACKGROUND

Claims 1-9 and 13-15 are drawn to compounds which are derivatives of known cyclohexapeptidyl compounds. These compounds are known in the art as echinocandins. Claims 10 and 11 are drawn to antibiotic compositions comprising the compounds of claim 1. Claim 12 is drawn to a method of administering a therapeutic amount of a compound set forth in claim 1 to a mammal to control microbial infection.

The compounds that were starting materials for the production of the claimed compounds are echinocandin hexapeptidyl compounds extracted from microbial fermentates. These parent compounds and their antibiotic activity were known prior to the filing date of this application.

#### DISCUSSION

##### Obviousness-type Double Patenting

Claims 1-15 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as lacking patentable distinction over (1) Claims 1-17 or (2) Claims 1-4 or (3) Claims 3-20 or (4) Claims 4-7 or (5) Claims

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1-11 and 13 or (6) Claims 1-10 or (7) Claims 1-9 of copending applications (1) 07/936,558; (2) 07/963,332; (3) 07/775,774; (4) 07/960,983; (5) 07/936,531; (6) 07/936,434; and (7) 07/959,948; respectively.

With respect to application Serial Number 07/960,983 this rejection is now moot in that this application has been abandoned. With respect to application Serial Number 07/775,774 and application Serial Number 07/936,434 this rejection is no longer provisional in that these applications have issued as U.S. Patent # 5,430,018 and U.S. Patent # 5,348,940, respectively.

The Appeal Brief acknowledges this rejection on page 4, however no argument is presented with respect to the merits of this rejection. In that no arguments have been presented by appellants as to why the examiner's rejection is erroneous, we summarily affirm this rejection.

In the Appeal Brief on page 4, appellants "requested that the Examiner hold any rejection on these grounds in abeyance until there is an indication of allowable subject matter."

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Appellants should note that an examiner does not have the authority to grant such a request. As explained in the Manual of Patent Examining Procedure, MPEP (6th edition, Rev. 3, July 1997) Section 1206, page 1200-8:

Appellants must traverse every ground of rejection set forth in the final rejection. Oral argument at the hearing will not remedy such a deficiency in the brief. Ignoring or acquiescing in any rejection, even one based upon formal matters which could be cured by subsequent amendment, will invite a dismissal of the appeal as to the claims affected. If this involves all of the claims, the proceedings in the case are considered terminated as of the date of the dismissal. Accordingly, any application filed thereafter will not be copending with the application on appeal.

In this application we consider appellants' comments to be an acquiescence on the merits. We are loathe to dismiss the appeal given the particular facts of this case, specifically the examiner's handling of the issue. The examiner failed to alert appellants to the consequences of an acquiescence in a rejection and to extend the opportunity to submit a complete Appeal Brief, and the comments made in the Examiner's Answer in this regard, which would give the impression that no more



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need be said by appellants in relation to the obviousness-type double patenting rejection at this stage of prosecution.

Rejections based on 35 U.S.C. § 103

Claims 1-15 stand rejected under 35 U.S.C. § 103 over Schmatz alone or in the alternative over '310 Pat. or '067 Pat. in combination with Michel.

The examiner's grounds of rejection are set forth on pages

4 and 5 of the Examiner's Answer to which we refer for the examiner's presentation of the reasons for rejection.

Schmatz discloses a genus of compounds which is inclusive of a number of species contained within the genus of claim 1 herein, with the exception of the hydroxyproline residue. Schmatz discloses a 3-hydroxy-4-methylproline, while the instantly claimed compounds do not contain a methyl group on the 4th carbon of the proline residue. Appellants pointed to this distinction in response to the first action and submitted two declarations pursuant to 37 CFR § 1.132. The declarations address properties of hexapeptidyl echinocandin derivatives

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which compare an echinocandin derivative with 4-methyl-3-hydroxyproline as the sixth residue against 19 compounds which are echinocandin derivatives with 3-hydroxyproline residues as the sixth residue. The examiner responded in the Final Rejection (Paper #9, pages 2 and 3) taking the position that the use of a broken line, in association with the methyl group of the hydroxyproline residue at columns 33 and 34 of Schmatz, suggested that the methyl can be a leaving group or that it can be cleaved. The examiner also stated at page 3 of the Final rejection that:

Further, it is well established in the art that a hydroxyproline residue containing a methyl or a hydrogen atom (i.e., desmethyl) are known to be functionally equivalent. ...Thus, applicants' arguments, the declarations of Mr. Bartizal, Jr. and Balkovec are of no probative value and are insufficient to overcome the 103 rejection since the comparison is not done with the disclosure identical (not similar) to that of the reference.

The examiner takes the same position with respect to '310 Pat., '067 Pat. and Michel, because these publications also depict dotted lines in association with the methyl group on

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the hydroxyproline residue of the hexapeptidyl compounds that they each disclose.

In the Appeal Brief, at page 3, appellants urge that the references depict tapered dashed lines from the pyrrolidine ring to the methyl group so as to indicate the stereochemistry of the compound and not any potential cleavage of the methyl group in question. The examiner does not controvert this in the Examiner's Answer.

The question is then raised as to whether the cited art is enabling for a method of making compounds which do not have a 4-methyl-3-hydroxyproline residue. Appellants state on page 4 of the Appeal Brief that "the art cited against the instant application ... does not teach a method of selectively removing the methyl group."

In the response to arguments, on pages 6 and 7 of the Examiner's Answer, reference is made to Schwartz, U.S. Patent 5,202,309. The Schwartz patent referred to was submitted by appellants in an Information Disclosure Statement filed after the Appeal Brief. In the paragraph bridging pages 6 and 7 of the Examiner's Answer the examiner states:

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Schwartz... teaches that both of these compounds are natural products of the same organism wherein the individual components of the natural product are separated from one another by methods commonly employed in the art such as fractionation, chromatography, etc. Therefore, one having ordinary skill in the art, at the time of the invention, would therefore be apprised of how to make a compound from a natural product containing either a non-methylated hydroxy Pro or methylated hydroxy Pro by employing procedures clearly known in the art of separating individual components from antibiotics of the type presently claimed.

It is clear from the examiner's discussion of this publication that it forms part of the evidence in support of a holding that

any or all of the claims would have been obvious. As the court

stated in In re Hoch, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n.3 (CCPA 1970):

Appellant complains that although neither of [the newly cited references] is mentioned in the statement of either of the appealed rejections and although this fact was pointed out in appellant's brief below, the board approved of their use by the examiner "as suggesting that [appellant's] compounds would

exert herbicidal action" and characterizing this as a use in a "minor capacity" (emphasis added) to "further support the rejection." Appellant's complaint seems to be justified, and if we did not find the rejections based solely on Molotsky and the French patent to be sound, we might well feel constrained to reverse the decision of the board. Where a reference is relied on to support a rejection, whether or not in a "minor capacity," there would appear to be no excuse for not positively including the reference in the statement of the rejection.

We do not consider the Schwartz reference to have been cited in the rejection before us, particularly since the examiner failed to indicate inclusion of the reference in the rejection and specifically indicated on page 3 of the Examiner's Answer that no "new prior art has been applied in this examiner's answer." Thus, we consider the issue of whether any of Schmatz, '310 Pat., '067 Pat. or Michel enable a method of making a compound which lacks a methyl at the fourth carbon of the hydroxyproline residue of the hexapeptidyl compounds disclosed by the references. Each of these references disclose obtaining the core cyclic hexapeptidyl compounds from microbial fermentates. In these references there is no discussion of culturing the exemplified microorganisms or other strains so as to obtain mixtures of cyclic hexapeptidyl

compounds which include variants which lack the methyl group in the hydroxyproline residue. While there is a statement in Michel, at page 1, lines 21-22 to the effect that the starting fermentates are mixtures of variant compounds there is no indication that the desmethyl variant is one of those known to be present in the microbial fermentate. The exemplified variants in Michel do not include the desmethyl variant. There is no teaching of removal of this methyl group either. Thus, we conclude that the cited references fail to provide any evidence that one of ordinary skill in the art would have been enabled to prepare the compounds of the cited prior art without a methyl on the fourth carbon of the hydroxyproline residue. Thus, the rejections presented under 35 U.S.C. § 103 are reversed.

#### Other Issues

We make note of a potential rejection under 35 U.S.C. § 103 based on the disclosure of Schmatz of echinocandin derivatives that are so closely related to the claimed compounds as to differ only in the lack of a methyl group in the hydroxyproline residue, coupled with the disclosure of the Schwartz reference discussed above, as to the existence of

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variants in echinocandin-containing fermentates of microorganisms of the species *Zalerion arboricola*, as well as methods of enriching the fermentate with respect to desmethyl variants and means of separating the variants from each other. While provisions exist for the presentation of such a rejection by this panel, we decline to make the necessary findings of fact in this case and consider that it is more prudent for the examiner to do so in the first instance. The examiner should conduct a claim-by-claim analysis of the differences between the claims and the prior art, should consider the level of skill of the ordinary artisan at the time of the invention and decide whether a *prima facie* case of obviousness exists. We also note the declarations of Dr. James Balkovec and Dr. Kenneth F. Bartizal, Jr. filed previously in this record as Paper Nos. 7 and 8, respectively. This evidence appears to be relevant and may well provide an adequate rebuttal, at least with respect to some of the claimed compounds, to any consideration as to whether the claimed compounds, compositions and method are obvious in view

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of the prior art. The examiner should carefully review this evidence.

## Conclusion

The decision of the examiner refusing to allow claims 1-15 under the judicially created doctrine of obviousness-type double patenting is affirmed.

The decision of the examiner refusing to allow claims 1-15 under 35 U.S.C. § 103 is reversed.

No time period for taking subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

**AFFIRMED**

SHERMAN D. WINTERS )  
Administrative Patent Judge )  
 )  
 )  
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	)	BOARD OF PATENT
CAMERON WEIFFENBACH	)	APPEALS
Administrative Patent Judge	)	AND
	)	INTERFERENCES
	)	
	)	
	)	
ELIZABETH C. WEIMAR	)	
Administrative Patent Judge	)	

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ECW/jrg

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APJ WEIMAR

APJ WINTERS

APJ WEIFFENBACH

DECISION: **AFFIRMED**

Typed By: Jenine Gillis

**DRAFT TYPED:** 14 Jul 99

**FINAL TYPED:**